available at www.sciencedirect.com journal homepage: www.europeanurology.com/eufocus





Editorial

## Mental Illness and Bladder Cancer Patients: The Time for Assertive Intervention Is Now

Zachary Klaassen a,b,\*, Soum D. Lokeshwar, Amy Lowery-Allison, Christopher J.D. Wallis d

<sup>a</sup> Division of Urology, Department of Surgery, Medical College of Georgia, Augusta University, Augusta, GA, USA; <sup>b</sup> Georgia Cancer Center, Augusta, GA, USA; <sup>c</sup> Miller School of Medicine, University of Miami, Miami, FL, USA; <sup>d</sup> Division of Urology, Department of Surgery, Princess Margaret Cancer Centre, University Health Network, Toronto, Canada

Bladder cancer (BC) patients are the most comorbid we encounter in urologic practice. In addition to medical comorbidities, there is emerging evidence that these patients also have significant psychiatric comorbidities, which may be present before BC diagnosis or develop subsequently [1]. To assess the influence of premorbid mental illness (MI), Sathianathen and colleagues [2] used the Surveillance, Epidemiology, and End-Results (SEER)-Medicare database to assess patterns of care and survival outcomes among patients diagnosed with BC with a preexisting MI, as reported in this issue of European Urology Focus. Among 66 476 patients, 6.7% had a pre-existing MI. These patients experienced worse management and had inferior outcomes throughout the disease process: they had worse disease at presentation, suggesting diagnostic delays; were less likely to receive curative treatment or neoadjuvant chemotherapy (NAC) for muscle-invasive BC (MIBC); experienced significant delays in receipt of radical cystectomy (RC); and had higher risk of cancer-specific mortality (CSM) and all-cause mortality (ACM).

In this study, BC patients with pre-existing depression were more likely to present with metastatic disease (odds ratio 1.17, 95% confidence interval [CI] 1.0–1.36) compared to those with no MI. This is in line with previous work from Western Australia noting that the proportion of cancer with metastases at presentation was significantly higher among psychiatric patients (7.1%, 95% CI 6.5–7.8%) than in the general population (6.1%, 95% CI 6.0–6.2%) [3]. According to Sathianathen et al [2], not only were patients with MIBC and MI less likely to receive RC or NAC but the mean time to RC from the date of diagnosis was also lower for patients

with severe MI than for those without MI (1.5 vs 3.9 mo; p < 0.001). Furthermore, the delay in RC was also prolonged for those with anxiety (4.3 mo) and anxiety/depression (3.2 mo). From previous work by Gore et al [4] we know that compared to those undergoing RC within 4–8 wk, there was a significant increase in CSM (hazard ratio [HR] 2.0) for those experiencing a delay of 12–24 wk, a category to which nearly every patient with MI in this study belonged.

The finding of worse CSM (HR 1.35, 95% CI 1.14-1.61) and ACM (HR 1.69, 95% CI 1.54-1.84) among patients with BC and MI in this SEER-Medicare study was recently confirmed by work we carried out using a comprehensive, populationbased sample from Ontario, Canada [5]. Among 29 884 patients with BC, compared to patients with no psychiatric care in the 5 yr before a BC diagnosis, those with prediagnosis psychiatric care utilization had worse CSM with increasing intensity of psychiatric care: outpatient psychiatric care, HR 1.09 (95% CI 1.03-1.14); psychiatric emergency department evaluation, HR 1.29 (95% CI 1.02-1.64); and inpatient psychiatric admission, HR 2.18 (95% CI 1.62-2.93). Similar results were noted for evaluation of ACM. In fact, among ten solid organ malignancies assessed, along with colorectal cancer, the effect of prediagnosis psychiatric care utilization on CSM and ACM was more profound among patients with BC.

Suicide awareness in the general population has recently improved with the help of media attention and several initiatives encouraging individuals at risk to seek appropriate help. Although suicidality may affect any age and gender, patients with BC (typically older, white, sometimes widowed men) are particularly at risk. Previous work using

DOI of original article: https://doi.org/10.1016/j.euf.2019.02.007.

\* Corresponding author. Division of Urology, Department of Surgery, Medical College of Georgia, Augusta University, 1120 15th Street, Augusta, GA 30912, USA. Tel. +1 706 7219977; Fax: +1 706 7212548.

E-mail address: zklaassen19@gmail.com (Z. Klaassen).

the SEER database suggested that the risk of suicide among BC patients is nearly three times higher than in the general population and more than six times higher for men [6]. Furthermore, unmarried BC patients (vs married: HR 1.74) and Caucasians (vs Black: HR 2.22) are more likely to die of suicide [7]. However, the nature of the association between BC diagnosis and suicide is unknown, as no studies to date have accounted for psychiatric comorbidities.

So why do these patients with BC and MI do so poorly? First, the stress from MI may result in biological changes that portend worse cancer diagnosis and outcome. This might be because of abnormalities in stress-related biological systems that can affect the immune surveillance of tumors [8]. Second, patients with psychiatric disorders are more likely to engage in behaviors detrimental to their health (ie, smoking and alcoholism [9]), which may impede their ability to follow guideline-specific follow-up, leading to worse outcomes. Alternatively, guideline-discordant care may stem from physician- rather than patient-driven factors. These patients may be less likely to undergo appropriate and timely diagnostic studies, such as cystoscopy for hematuria, which delays diagnosis. Sathianathen et al [2] demonstrated for the first time that patients with MIBC and MI experience a delay in timely RC; this suggests that these patients are probably marginalized and receive substandard, non-guideline-specific care. Introspectively, perhaps as clinicians we contribute to this disparity, as these patients may be uncomfortable and/or difficult to manage.

Although prospective studies have been conducted to assess the wellbeing of BC patients using validated quality-of-life instruments (universally, quality of life is poor and these patients are depressed) [1], the time for prospective assertive intervention with rigorous assessment of efficacy of these interventions is now. We have ample literature and clinical intuition to understand that these are patients at high risk of depression, anxiety, and suicidality who are undergoing procedures that will affect how they look (eg, stoma), feel (depressed, anxious), and perceive themselves (eg, sexual dysfunction). Therefore, at our institution we are developing a prospective program whereby every new BC patient is screened by our psycho-oncology team as part of

our cancer survivorship model. Further intervention and follow-up, if necessary, will be delineated by our psychooncology providers. Ultimately, it is the responsibility of everyone in the health care team (physicians, nurses, social workers, stoma nurses, etc.) to work with BC patients, especially those with MI, to ensure that treatments and outcomes are optimized.

Conflicts of interest: The authors have nothing to disclose.

## References

- [1] Pham H, Torres H, Sharma P. Mental health implications in bladder cancer patients: a review. Urol Oncol 2019;37:97–107.
- [2] Sathianathen NJ, Fan Y, Jarosek SL, et al. Disparities in bladder cancer treatment and survival amongst elderly patients with a pre-existing mental illness. Eur Urol Focus 2019. http://dx.doi.org/10.1016/j.euf. 2019.02.007, pii: S2405-4569(19)30027-6 [Epub ahead of print] PMID: 30797737.
- [3] Kisely S, Crowe E, Lawrence D. Cancer-related mortality in people with mental illness. JAMA Psychiatry 2013;70:209–17.
- [4] Gore JL, Lai J, Setodji CM, Litwin MS, Saigal CS. Mortality increases when radical cystectomy is delayed more than 12 weeks: results from a Surveillance, Epidemiology, and End Results-Medicare analysis. Cancer 2009;115:988–96.
- [5] Klaassen Z, Wallis CJD, Goldberg H, et al. The impact of psychiatric utilisation prior to cancer diagnosis on survival of solid organ malignancies. Br J Cancer 2019. http://dx.doi.org/10.1038/ s41416-019-0390-0, [Epub ahead of print] PMID: 30837680.
- [6] Klaassen Z, Jen RP, DiBianco JM, et al. Factors associated with suicide in patients with genitourinary malignancies. Cancer 2015;121:Error: FPage (1864) is higher than LPage (1872)!.
- [7] Klaassen Z, Goldberg H, Chandrasekar T, et al. Changing trends for suicidal death in patients with bladder cancer: a 40+ year population-level analysis. Clin Genitourin Cancer 2018;16, 206–12.e1.
- [8] Reiche EM, Morimoto HK, Nunes SM. Stress and depression-induced immune dysfunction: implications for the development and progression of cancer. Int Rev Psychiatry 2005;17:515–27.
- [9] Perini G, Grigoletti L, Hanife B, Biggeri A, Tansella M, Amaddeo F. Cancer mortality among psychiatric patients treated in a community-based system of care: a 25-year case register study. Soc Psychiatry Psychiatr Epidemiol 2014;49:693–701.